# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



| Applicant's or agent's file reference | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
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| International Patent Classification (IPC) or both national classification and IPC | | |
| C07K14/705 | | |
| Applicant | | |
| STEINKASSERER, Alexander et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 13 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 21.06.2004 | 10.02.2005 |
| Name and mailing address of the international preliminary examining authority: | Authorized Officer |
| European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Böhmerova, E<br>Telephone No. +49 89 2399-7859 |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/12941

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

49-58 as originally filed

**Claims, Numbers**

1-28 received on 26.01.2005 with letter of 26.01.2005

**Drawings, Sheets**

1/20-20/20 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☒ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   *(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

   **see separate sheet**

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 18,28

   because:

   ☒ the said international application, or the said claims Nos. 18,28 relate to the following subject matter which does not require an international preliminary examination (specify):

   **see separate sheet**

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-11, 18-28 |
| | No: | Claims | 12-17 |
| Inventive step (IS) | Yes: | Claims | 1-11, 18-28 |
| | No: | Claims | 12-17 |
| Industrial applicability (IA) | Yes: | Claims | 1-17,19-27 |
| | No: | Claims | 18,28 |

2. Citations and explanations

**see separate sheet**

**R Item I**

**Basis of the report**

The amendments filed with the letter dated 26.01.2005 introduce subject-matter which extends beyond the content of the application as filed, contrary to Article 34(2)(b) PCT. The amendments concerned are the following: New claim 12 is directed to a soluble form of a member of the CD83 family of proteins (soluble CD83 protein) consisting of amino acids 20 to 144 of SEQ ID NO: 2, a fragment, dimeric form and/or functional derivative thereof. According to the applicant, the base for new claim 12 should be original claim 15. However, original claim 15 was directed to a soluble form of a member of the CD83 family of proteins (soluble CD83 protein) comprising amino acids 20 to 144 of SEQ ID NO:2. No support can be found for the soluble form of CD83 protein consisting of amino acids 20 to 144 of SEQ ID NO:2.

Consequently, the following opinion on novelty, inventiveness and industrial applicability has been made as if claim 12 was identical to the original claim 15, i.e. directed to the soluble CD83 protein comprising amino acids 20 to 144 of SEQ ID NO:2.

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 18, 28 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**Cited documents**

D1: WO-A-9729781
D2: US-A-5710262
D3: Protein Expression And Purification (04-2002), 24(3), 445-452
D4: Journal Of Experimental Medicine (17-12-2001), 194(12), 1813-1821
D5: International Archives Of Allergy And Immunology (20-10-2002), 129(2), 113-

118

D6: Gene, Elsevier Biomedical Press. Amsterdam, NI (1988), 67(1), 31-40

Unless indicated otherwise reference is made to the passages considered relevant in the search report.

**Novelty**

The applicant's arguments concerning novelty of the present claims have been taken into the consideration. However, the subject-matter of claims 12-17 is considered to lack novelty under Art. 33(1) and (2) PCT for the following reasons:

D1 discloses a method of stimulating a humoral immune response comprising administering DNA encoding CD83, preferably DNA having nucleotide sequence encoding an amino acid sequence 1 through 124 or SEQ ID NO: 2, or CD83 peptide or a fragment thereof, preferably the extracellular domain of CD83 having an amino acid sequence of amino acids 1 - 124 of SEQ ID NO: 2 which is identical to amino acids 20-144 of SEQ ID NO: 2 according to the present application. D1 expressly discloses a CD83 peptide having an amino acid sequence of amino acids 1 through 124 of SEQ ID NO: 2 (claim 6 (a), claim 7). DNA coding the soluble CD83 was cloned to an expression vector pDC409 and was expressed in monkey kidney cell line (Example 1). Soluble CD83 or DNA coding said soluble CD83 was used for stimulating a humoral immune response. This disclosure of D1 anticipates novelty of present claims 12,14-17,

D2 discloses a nucleic acid encoding HB15 (CD83) having the amino acid sequence of SEQ ID NO: 2 which is identical to the amino acid sequence SEQ ID NO: 2 of the present application. According to D2, the extracellular domain of HB15 consists of amino acids 1-125 of SEQ ID NO: 2, i.e. it comprises a signal sequence of 19 amino acids. However the extracellular domain of CD83 according to the present application comprises amino acids 20 to 144 of the identical sequence, i.e. it does not comprise the signal sequence of 19 amino acids. Consequently, the soluble form of CD83 according to the present application appears to differ over that of D2 and novelty of present claims over the disclosure of D2 can be acknowledged.

D3 and D4 disclose recombinant expression of the extracellular CD83 domain - hCD83ext. The method of cloning, expression and purification of hCD83ext is identical

with that disclosed in the present application: the same primers were used, the amplified fragment was subcloned to the same sites of the same vector and expressed in the same *E.coli* strain, the same purification protocol was employed. The resulting extracellular CD83 domain appears to comprise amino acids 20-145, it is however considered to fall within the present definition of the soluble CD83 according to claim 12 (see Item I above). Therefore, the disclosure of D3 and D4 anticipates novelty of present claims 12, 14-17.

D3 and D4 do not explicitly disclose a soluble CD83 which further has functional sequences attached to its N-terminus. as claimed in claim 13 (preferably the sequence comprising amino acids 20-145 of the CD83 with additional amino acids Gly-Ser-Pro-Gly at the N-terminus). However, such a construct appears to be the result of the cleavage of the fusion protein GST-hCD83ext expressed from the vector pGEX-2T by thrombin (see D6, figure 1 depicting the thrombin cleaving site and surrounding regions of PGEX-2T). In view of D6, the disclosure of D3 and D4 is considered to be prejudicial for novelty of claim 13.

D5 discloses that the soluble extracellular CD83 domain (hCD83ext) suppresses dendritic cells-mediated T cell proliferation and is immunosuppressive both *in vivo* and *in vitro*. D5 however does not disclose the exact amino acid sequence of said hCD83ext. The use of hCD83ext in the treatment or prevention of medical conditions is not disclosed. Consequently, D5 does not anticipate novelty of the present claims.

The subject-matter of claims 1-11, 18-28 is considered to be new under Article 33(1) and (2) PCT.

**Inventive step**

As the subject-matter of claim 12-17 is considered as lacking novelty, no inventiveness can be acknowledged at this stage.

The subject-matter of claims 1-11, 18-28 is considered to involve an inventive step under Art. 33(1) and (3) PCT, the reasons being as follows:

The problem to be solved by the present application can be defined as to provide a medicament for the treatment of diseases caused by the dysfunction or undesired function of cellular immune response involving T and/or B cells, such as allergies,

asthma, transplant rejection etc..

The solution proposed by claims 1-11, 18 is the use of soluble CD83 protein comprising amino acid residues 20 to 144 of SEQ ID NO:2 or a nucleic acid or a vector coding such soluble CD83 protein. The solution proposed by claims 19-28 is the use of soluble monomeric CD83 protein wherein one or more of the cysteine residues have been substituted, or a nucleic acid or a recombinant expression vector encoding such soluble CD83 protein. The proposed solutions appear to solve the above defined technical problem as proven by the results of Example 5 and additional experimental data provided by the applicant. None of the prior art documents appears to propose the use of the soluble extracellular CD83 protein for the treatment of the above defined diseases.

**Industrial applicability**

Subject-matter of claims 1-17, 19-27 is considered to be industrially applicable under Art. 33(1) and (4) PCT.

For the assessment of the present claim 18, 28 on the question whether it s industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

# IDENFIFICATION OF A FUNCTIONAL ACTIVE SOLUBLE MONOMERIC CD83 MUTANT.

## COMPARATIVE ANALYSIS OF MONOMERIC AND DIMERIC ISOFORMS REVEAL THAT THE MONOMERIC FORM IS BIOLOGICALLY MORE ACTIVE

**Summary**

Recently, we reported that soluble CD83 has a strong immunosuppressive activity *in vitro* as well as *in vivo*. Sequence alignment of CD83 between different species and molecular homology modeling revealed the presence of an uneven number of five cysteines in the extracellular Ig-domain of the protein. This opens the possibility that four cysteines are involved in the formation of two intramolecular disulfide bonds and a possible involvement of the remaining fifth cysteine in the formation of an intermolecular covalent disulfide bond, leading to the dimerization of the extracellular protein domains. SDS-PAGE analysis using recombinant human soluble CD83 under non-reducing conditions confirmed a dimeric form of the protein. Using recombinant mutational analyses, were the fifth cytosine at amino acid position 129 was mutated to a serine, we could prove that the fifth cysteine residue was indeed necessary for the dimerization (see Figure 1).

Comparison of the inhibitory function (using the MLR assay) of the mutant monomeric form of soluble CD83 (hCD83ext_mut129_CtoS) with the wild type dimeric form of soluble CD83 (hCD83ext) revealed that the inhibitory function of the mutant form was 10 % better when compared with the wild type form (see Figure 2). Thus, we generated a new previously not known monomeric soluble CD83 isoform with better immunosuppressive activities.

**Materials and Methods**

*Cloning of the mutant soluble CD83 isoform (hCD83ext_mut129_CtoS) in Escherichia coli.*

The mutant extracellular domain of human CD83 (amino acids 20-145) was PCR-amplified using the following primer set: sense- pGEX2ThCD83: 5`-TCCCCCCGGGAACGCCGGA-GGTGAAGGTGGCT-3`and antisense-CD83extra_mutantCtoS: 5`-AATTAGAATTCTCAA-ATCTCCGCTCTGTATTTCTTAAAAGTCTCTTCTTTACGCTGTGCAGGGGAT-3` (MWG-Biotech AG). The antisense primer inserts a g to c nucleotide transversion which leads to an amino acid exchange of cystidine to serine at the amino acid position 129. The amplified cDNA fragment was subcloned into the SmaI and EcoRI sites of the expression vector pGEX2T (Amersham Pharmacia Biotech) resulting in the plasmid pGEX2ThCD83ext_mut129_CtoS and was transformed into the E.coli strain BL21(DE3) pLysS (Novagen, Schwalbach, Germany). The correct nucleotide sequence was verified by sequencing.

*Expression and Purification of hCD83ext_mut129_CtoS*

The mutant Protein hCD83ext_mut129_CtoS was expressed in BL21(DE3)pLysS (Novagen) and purified as described previously described for the dimeric wild type hCD83ext isoform

*SDS-PAGE- and immunoblotting analyses*

HPLC-purified proteins were separated on 15% sodium dodecyl sulfate (SDS)-polyacrylamide gels and blotted onto nitrocellulose filters. The membranes were blocked with 5% dry milk in TBST (20 mM Tris-HCl, pH 7.5, 150 mM NaCl, 0.05% Tween 20) for 1 h. Incubation with the monoclonal anti-CD83 antibodies (1:100 CD83-1G11) (3) was performed overnight at 4°C or for 1 h at room temperature in blocking solution. After washing three times with TBST, the filters were incubated for 1 h at RT with a 1:20000 dilution of the rabbit-anti-rat IgG antibody coupled to horseradish peroxidase (Dianova, Hamburg,

Germany). Immunoreactive bands were visualized using an epichemiluminescence Western blotting system (Amersham Pharmacia Biotech, Freiburg, Germany) according to the manufacturer's protocol.

*Surface Plasmon Resonance(BIACORE) Analysis*

A BIACORE X system and CM5 sensor chips (research grade) were used for binding studies (BIACORE AB). GST or GST-hCD83ext fusion protein were immobilized on the chip surface using the BIACORE GST-kit for fusion capture (BIACORE AB) according to the manufacturer's instructions. Proteins were diluted to concentrations between 5-10 µg/ml in HBS-EP buffer (10 mM Hepes pH 7.4, 150 mM NaCl, 3 mM EDTA, 0,005% polysorbate 20) and captured on the chip at a flow rate of 5 µl/min, until a change of at least 1.000-1.500 resonance units (RU) was detectable. The RU baseline was then allowed to stabilize for at least 15 min. For the determination of interactions, the hCD83ext or hCD83ext_mut129_CtoS proteins were diluted in HBS-EP buffer to a final volume of 80 µl and subsequently injected over both flow cells (flow cell 1: GST; flow cell 2: GST-hCD83ext) at a flow rate of 20 µl/min. The injected proteins were allowed to dissociate from the bound-protein during a wash-step in which HBS-EP buffer was injected for an additional 60-90 sec. To completely remove bound proteins, the chip was regenerated by using the GST-kit regeneration solution capture (BIACORE AB) according to the manufacturer's instructions. Upon completion of the binding profiles, the responses from all flow cells were baseline corrected. The response from the reference cell (flow cell 1: GST) was subtracted from the response of flow cell 2 (GST-hCD83ext) to correct for refractive index changes, non-specific binding and instrument drift. All experiments were performed at RT.

*T Cell Proliferation Assay*

The CD4 and CD8 positive (NAF) T cells were stimulated at different ratios with mature allogeneic DC in a final volume of 200 µl/well RPMI 1640 supplemented with 5% human serum from a single AB donor in 96-well plates. These mixed leukocytes were treated with hCD83ext (10µg/ml), hCD83ext_mut129_CtoS (10µg/ml) or left untreated (MOCK) and incubated for 4 days at 37°C. Then the cells were pulsed with 1 µCi/well [$^3$H] thymidine (Amersham) for 16 h. The culture supernatants were harvested onto glass fiber filters (Printed Filtermat A; Wallac, Turcu, Finland) by using an ICH-110 harvester (Inotech, Dottikon, Switzerland), and [$^3$H] thymidine incorporation was determined using a microplate counter (Wallac).

**Results**

*CD83 is a disulfide-linked homodimeric protein*

To investigate if the extracelluar domain of CD83 can indeed form homodimers via disulfide bonds the recombinant human soluble CD83 domain (hCD83ext) was further analyzed using SDS-PAGE analyses under reducing and non-reducing conditions (Fig. 1A) followed by Western blotting using the anti-CD83 antibody CD83-1G11 (Fig. 1B). Interestingly, in the absence of reducing agents, the soluble CD83 molecule formed a dimer, double the size of the monomer (see Fig. 1A lane 5 and 1B lane 4), indicating that all intra-and interchain disulfide bonds are intact. For comparison under reducing conditions the molecule did not form any dimers anymore (see Figure 1A lane 4 and 1B lane 3).

In order to determine which cysteine residue is responsible for the dimerization of hCD83ext a mutant form of hCD83ext with a g to c nucleotide transversion which lead to an amino acid exchange of the fifth cystein at position 129 into a serine residue was cloned (hCD83ext_mut129_CtoS), expressed in *E. coli* and purified and compared with the hCD83ext wild type protein. As shown in figure 1A (lane 1 and 2) the mutant form of CD83

showed a stable monomeric band under reducing as well as under non-reducing conditions. This band was identical to the hCD83ext wildtyp protein band analysed under reducing conditions. The specificity of the mutant CD83 protein was again confirmed by Western blot analyses (see Fig. 1B, lane 1 and 2). Thus form these data we conclude, that the fifth carboxyterminal cystein at position 129 of the extracellular CD83 domain is necessary for the formation of homodimers.

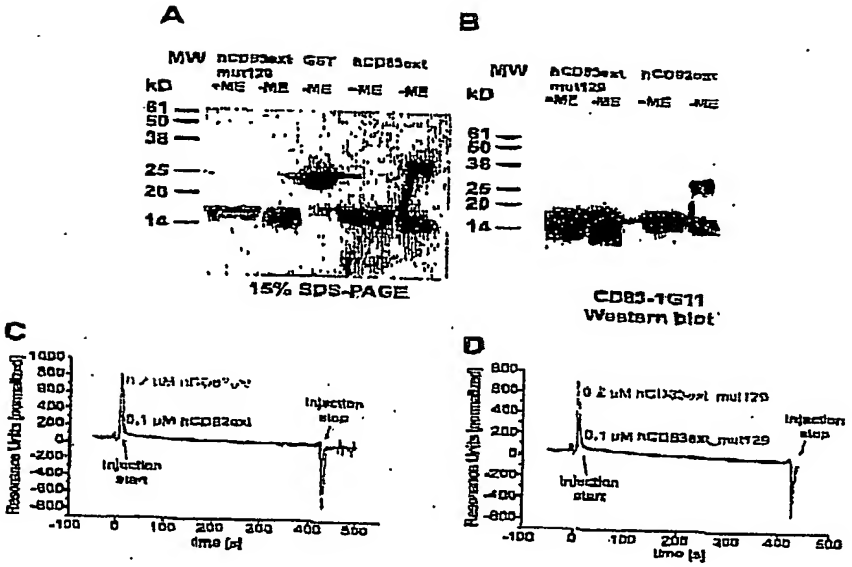
In order to investigate if also non-covalent interactions between CD83ext molecules are possible, surface plasmon resonance responses were measured in real time using a Biacore X system. Recombinant GST-hCD83ext was immobilized via anti-GST antibody coupling as ligand onto a CM5 sensor chip. Analytes were different concentrations of hCD83ext or hCD83ext_mut129_CtoS protein diluted in PBS. Data were analyzed with the BIAevaluation program 3.0 (Biacore AB). As shown in Fig. 1C and 1D, Biacore analyses did not indicate any interactions of hCD83ext with the hCD83ext wild type form (Fig. 1C) nor with the mutant hCD83ext_mut129_CtoS monomeric form (Fig. 1D). Under our experimental conditions (RT, PBS) non-covalent CD83 oligomerization was not detectable.

*Inhibition of DC mediated allogeneic T cell proliferation using mutant- monomeric soluble CD83*

Regarding the functional properties of wild type soluble CD83 we previously reported, that it strongly inhibits DC-mediated allogeneic T cell proliferation. Hence, we studied the inhibitory effect of the mutant- monomeric CD83 protein and compared it with the wild type CD83 protein using a mixed leukocyte reaction (MLR) assay. Surprisingly, the mutant monomeric CD83 protein inhibited T cell proliferation even better then the soluble wild type

protein (see Fig. 2). Thus, we generated a new previously not known monomeric soluble CD83 isoform with better immunosuppressive activities.

**Figure 1:**



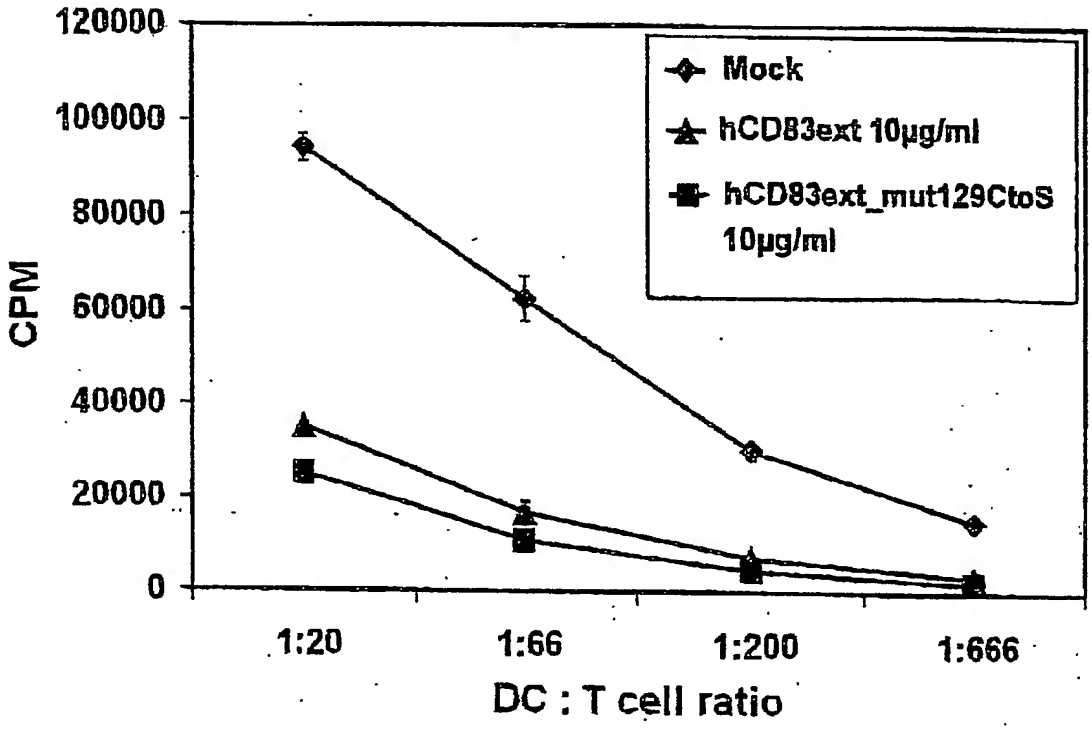

*Analyses of mutant and wild type isoforms of soluble CD83.*

(A) SDS-PAGE analyses comparing mutant and wild type form of soluble CD83 under reducing (+ME) and non-reducing conditions (-ME). Recombinant human hCD83ext (wild type) and hCD83ext_mut129_CtoS (mutant) protein were analyzed using SDS-PAGE. To identify possible oligomeric forms of CD83 2-mercaptoethanol has been omitted from the sample buffer (-ME). GST was used as a control in order to exclude that the upper band is a contaminations due to the GST-tag. These data clearly show that the mutant isofrom of soluble CD83 is a monomer, while the wild type isoform is a dimmer.

(B) Western blot analyses using an anti-CD83 specific monoclonal antibody (CD83-1G11). Following the protein separation on a 15% SDS-PAGE, the recombinant proteins were electro-blotted onto nitrocellulose membranes. The specificity of the protein bands were confirmed with the anti-CD83 mAb (CD83-1G11). Again, these data clearly show that the mutant isofrom of soluble CD83 is a monomer, while the wild type isoform is a dimmer.

(C and D) Sensogramm analyzing the non-covalent interactions between two hCD83ext or CD83ext and hCD83ext_mut129CtoS molecules. The GST-hCD83ext fusion protein was immobilized on the surface of a CM5 sensor chip. Binding of different concentrations (0.1µM and 0.2µM) of hCD83ext (C) or hCD83ext_mut129CtoS (D) to immobilized hCD83ext was detected by changes in resonance units (RU) over time. The sensograms shown were obtained after reference (GST) subtraction.

**Figure 2:**




*The mutant monomeric soluble CD83 isoform (hCD83ext_mut129_CtoS) has a higher inhibitory activity then the wild type soluble CD83 isoform (hCD83ext).*

MLR analysis: $CD4^+$ and $CD8^+$ human T cells were stimulated at different ratios with mature allogeneic DC in 96-well plates. These mixed leukocytes were treated with equal concentrations of hCD83ext, hCD83ext_mut129_CtoS, or left untreated (Mock) and incubated for 4 days at 37°C. Then the cells were pulsed with 1 µCi/well [$^3$H] thymidine (Amersham) for 16 h and analyzed. The hCD83ext_mut129_CtoS mutant showed a higher inhibitory effect when compared with the wild type hCD83ext protein.

PCT/EP03/12941
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JH/ml
January 26, 2005

**Claims**

1. Use of a soluble form of a member of the CD83 family of proteins (soluble CD83 protein) comprising amino acid residues 20 to 144 of SEQ ID NO:2, a fragment, a dimeric form and/or a functional derivative thereof, for the production of a medicament for the treatment or prevention of a disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells.

2. The use of claim 1, wherein the soluble CD83 protein further
(a) has one or more amino acid residues derived from the neighbouring intracellular domain at its C-terminus, preferably the soluble CD83 protein comprises amino acid residues 20 to 145 of SEQ ID NO:2; and/or
(b) has functional sequences attached to its N-terminus, preferably functional sequences of up to 10 amino acid residues, and most preferably carries at the N-terminus the additional amino acids Gly-Ser-Pro-Gly.

3. The use of claim 1, wherein the soluble form of the CD83 protein comprises amino acid residues 1 to 130 of SEQ ID NO:8.

4. The use of claim 1, wherein the soluble CD83 protein is a dimer, preferably a homodimer connected through one or more of the cysteine residues of the monomeric form of the soluble CD83 protein.

5. The use of claim 4, wherein the soluble CD83 protein is as defined in claim 2 or 3 and/or the homodimer is connected through the fifth cysteine residue of the monomeric form of the soluble CD83 protein.

6. The use of claim 1, wherein the soluble CD83 protein is a monomeric CD83 protein, preferably the soluble CD83 is as defined in claim 2 or 3.

7. The use according to anyone of claims 1 to 6, wherein the medicament is suitable
(a) for the treatment or prevention of paralysis, preferably for the treatment or prevention of paralysis associated with progressive multiple sclerosis; and/or
(b) for transcutan, intracutan, subcutan or systemic admministration together with a specific antigen.

8. The use of a nucleic acid or vector having a DNA fragment encoding a CD83 protein as defined in any one of claims 1 to 6 for the production of a medicament for the treatment or prevention of a disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells.

9. The use of claim 8 wherein the DNA fragment comprises nucleotides 58 to 432 of SEQ ID NO:1.

10. The use of claim 8 or 9 wherein the medicament is suitable for downregulation on RNA and or protein level of the expression of CD83 in mammals.

11. The use of claim 1 or 8, wherein said disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells is selected from the group consisting of allergies, asthma, rejection of a tissue or organ transplant, autoimmune syndromes such as myasthemia gravis, multiple sclerosis, vasculitis, cronic inflammatory bowl diseases such as Morbus Crohn or colitis ulcerosa, HLA B27-associated autoimmunopathis such as Morbus Bechterew, and systemic lupus erythematosis, skin diseases such as psoriasis, rheumatoid arthritis, insulin-dependent diabetes mellitus and AIDS.

12. A soluble form of a member of the CD83 family of proteins (soluble CD83 protein) consisting of amino acids 20 to 144 of SEQ ID NO:2, a fragment, dimeric form and/or functional derivative thereof.

13. The soluble CD83 protein of claim 12 wherein the protein further has functional sequences attached to its N-terminus, preferably functional sequences of up to 10 amino acid residues, and most preferably carries at the N-terminus the additional amino acids Gly-Ser-Pro-Gly.

14. A nucleic acid or recombinant expression vector encoding the CD83 protein of claim 12 or 13, said nucleic acid or recombinant expression vector preferably comprising nucleotides 37-417 of SEQ ID NO:7.

15. A pharmaceutical composition comprising the soluble CD83 protein of claim 12 or 13, or the nucleic acid or vector of claim 14.

16. A prokaryotic or eukaryotic host cells transformed/transfected with a nucleic acid or a vector of claim 14.

17. A method for producing the soluble CD83 protein of claim 12 or 13, which comprises culturing a transferred/transfected prokaryotic or eukaryotic host cell according to claim 16.

18. A method for treating or preventing a disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells comprising administering the person in need for such treatment a pharmaceutically suitable amount of the soluble CD83 protein as defined in any one of claims 1 to 6 or 12 to 13, or of the nucleic acid r vector as defined in any one of claims 8 to 9 or 14.

19. A soluble form of a member of the CD83 family of proteins being a monomeric CD83 protein wherein one or more of the cysteine residues have been substituted by same or different small and/or polar amino acid residues.

20. The monomeric soluble CD83 protein of claim 19, wherein

(i) the small and/or polar amino acid residues are selected from serine, alanine, glycine, etc., preferably is serine; and/or

(ii) the soluble CD83 further has one or more amino acid residues derived from the neighbouring intracellular domain at its C-terminus, preferably the soluble CD83 protein comprises amino acid residues 20 to 145 of SEQ ID NO:2; and/or;

(iii) the soluble monomeric CD83 further has functional sequences attached to its N-terminus, preferably functional sequences of up to 10 amino acid residues, and most preferably carries at the N-terminus the additional amino acids Gly-Ser-Pro-Gly; and/or

(iv) the soluble form of the CD83 protein comprises amino acid residues 1 to 130 of SEQ ID NO:8; and/or

(iii) one cysteine residue, preferably the fifth cysteine residue has been replaced.

21. The monomeric soluble CD83 protein of claim 19 or 20, where the soluble CD83 protein comprises amino acid residues 20 to 144 of SEQ ID NO:2, where the cysteine residue at position 129 has been replaced by a serine residue, or comprises amino acid residues 1 to 130 of SEQ ID NO:10.

22. A nucleic acid or recombinant expression vector encoding the CD83 protein according to any one of claims 19 to 21.

23. A prokaryotic or eukaryotic host cells transformed/transfected with a nucleic acid or a vector of claim 22.

24. A method for producing the soluble CD83 protein according to any one of claims 19 to 21, which comprises culturing a transferred/transfected prokaryotic or eukaryotic host cell according to claim 23.

25. A pharmaceutical composition comprising the soluble CD83 protein as defined in any one of claims 19 to 21, or the nucleic acid or vector as defined in claim 22.

26. Use of a monomeric soluble CD83 according to anyone of claims 19 to 21 or of the nucleic acid or vector of claim 22 for the production of a medicament for the treatment or prevention of a disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells.

27. The use of claim 26, wherein said disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells is selected from the group consisting of allergies, asthma, rejection of a tissue or organ transplant, autoimmune syndromes such as myasthemia gravis, multiple sclerosis, vasculitis, cronic inflammatory bowl diseases such as Morbus Crohn or colitis ulcerosa, HLA B27-associated autoimmunopathis such as Morbus Bechterew, and systemic lupus erythematosis, skin diseases such as psoriasis, rheumatoid arthritis, insulin-dependent diabetes mellitus and AIDS.

28. A method for treating or preventing a disease or medical condition caused by the dysfunction or undesired function of a cellular immune response involving dendritic cells, T cells and/or B cells comprising administering the person in need for such treatment a pharmaceutically suitable amount of the soluble CD83 protein according to any one of claims 19 to 21 or of the nucleic acid of claim 22.